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The Relation between Memory and Decision-Making in Multiple Sclerosis Patients

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Abstract

Background. Impairments in long-term and working memory are widespread in Multiple Sclerosis (MS), setting on in early disease stages. These memory impairments may limit patients' ability to take informed and competent medical decisions, too. In healthy populations, memory abilities predict decision quality across a wide range of tasks. These studies suggest that higher working memory capacity supports decisions in cognitively taxing tasks, whereas better semantic memory facilitates decisions in tasks requiring knowledge retrieval. In individuals with MS, previous studies have linked less accurate decisions to memory deficits and reduced executive functioning, too. However, these studies focussed on decisions under risk and did not broadly assess decision making skills. We aimed to fill this gap in a cross-sectional study. **Methods.** Hundred thirty-seven participants with MS were recruited during their stay in an MS specialized rehabilitation centre. In a first test session, participants completed a standardized test battery for working memory and semantic memory, the inventory for memory diagnostics. In a second test session, participants filled out the Adult Decision Making Competence battery (A-DMC). This version of the A-DMC measured decision making competence on five subscales: Resistance to

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Framing Effects, Under/Overconfidence, Applying Decision Rules, Consistency in Risk Perception, and Resistance to Sunk Cost Effects. In addition, participants were screened for depression and cognitive fatigue. **Results.** Working memory was impaired in most participants, whereas semantic memory was not impaired. To understand which memory abilities underlie distinct components of decision making in people with MS, we used structural equation modelling. Replicating previous findings in a healthy sample, working memory capacity was associated with the ability to recall semantic knowledge. Participants with lower working memory capacity were less resistant to framing effects and adhered to decision rules less. In contrast, participants with worse semantic memory assessed their own knowledge less accurately, perceived risks less consistently, and made more errors in applying decision rules. Cognitive fatigue and depression unlikely explain these relationships. **Conclusions.** Taken together, our study suggests that the memory problems, frequently reported in MS patients, may reach out to higher-order cognitive functions, such as decision making skills. Supporting shared decision-making and patient autonomy within MS thus requires to take memory impairments into account and to match the information provided to the patient’s memory abilities.

Keywords: Decision Making; Long-Term Memory; Short-Term Memory; Multiple Sclerosis; Shared Decision Making; Choice Behavior

1. Introduction

One of the most prevalent and earliest symptoms of MS are cognitive dysfunctions, such as short-term and long-term memory impairments, with prevalence rates of 43-70% [1, 2, 3]. Previous research has, however, often neglected
 5 consequences of memory impairments for well-being, quality of life, and patient decisions [4]. For instance, many patients prefer to take an active role in treatment decisions, especially those patients who experience more disabilities [5].

Importantly, cognitive abilities may interact with patients’ ability to take

10 informed and competent medical and life decisions. In healthy populations,
memory abilities have been shown to predict decision quality and decision mak-
ing skills across a wide range of cognitive tasks [6, 7, 8, 9, 10] and real-life settings
[11]. In persons with MS, worse decisions have been traced back to deficits in
processing speed, visual memory performance, reduced memory, and executive
15 functioning [12, 13]. Most studies on persons with MS focussed on a narrow
subset of decisions, namely decisions under risks [14, 13, 15] in which choice
outcomes are known and realized with a predefined probability. Yet, decision
making requires executing a variety of subprocesses: estimating the likelihood of
outcomes, evaluating decision outcomes, integrating outcomes and beliefs into
20 a decision, and metacognitive skills [6].

In healthy adults, working memory, the ability to simultaneously store and
manipulate information [16], likely underpins the evaluation of decision out-
comes and the accurate integration of outcomes and beliefs into a decision.
Specifically, evaluating decision outcomes requires to focus attention on the
25 relevant information and to ignore irrelevant information, whereas integrating
outcomes and beliefs requires mentally updating the information in working
memory [17]. In this vein, previous research has consistently shown that work-
ing memory predicts decision performance in tasks that require rule application
[7, 17, 8, 9] or that require to ignore how a problem is described or framed (Re-
30 sistance to Framing, [8]). Metacognitive skills, the ability to assess the quality
of one’s own knowledge and decisions, have been suggested to demand work-
ing memory [8], too. Especially, taking disconfirming evidence into account,
a cognitively taxing process, should reduce overconfidence and lead to better
calibrated judgments [18]. In contrast, semantic memory likely predicts perfor-
35 mance in decision tasks that demand a high amount of background knowledge
[8]. For instance, assessing risks consistently requires the knowledge of the laws
of probability and, thus, retrieval of knowledge from semantic memory. Simi-
larly, ignoring unrecoverable investments requires the normative knowledge that
future decisions should be independent of past costs. In line with this idea, se-
40 mantic memory is predictive of the ability to perceive risks consistently as well

as the ability to ignore unrecoverable investments [8]. We aimed to replicate these relationships in individuals with MS and to examine how individual differences in memory abilities relate to five aspects of decision making competence, as measured by the multi-dimensional Adult Decision-Making Competence battery (A-DMC, [6]).

Memory impairments in MS may be caused by comorbid diseases, such as depression, or disease-related symptoms, such as cognitive fatigue, too. Depression may adversely impact on working memory [19, 20], whereas cognitive fatigue has been related to alertness and vigilance [21]. If fatigue and depression impede memory performance, those impairments may in turn harm decision making skills.

2. Methods

2.1. Participants

Hundred thirty-seven participants with a MS diagnosis (98 women, 71.5%, $M_{Age} = 49.4$ years, $SD_{Age} = 10.4$ years, range: 19-76 years) were recruited during their stay in the Kliniken Schmieder Konstanz, Germany. The Kliniken Schmieder is a MS specialised neurological rehabilitation centre that admits MS patients for an interdisciplinary cognitive and physical rehabilitation treatment. To recruit participants, all incoming patients were screened for a MS diagnosis as the admission reason. Inclusion criteria were: a confirmed MS diagnosis according to the revised McDonald criteria [22], Age ≥ 18 , native German speakers, no severe visual deficits or other neurological diseases. Patients with a relapse or steroid treatment within the last four weeks were excluded. All MS patients fulfilling these criteria were consecutively asked to participate in the study.

Educational background was comparable to the average population (18.2% Hauptschule, i.e. degree after grade 9, 44.5% Realschule, i.e. degree after grade 10, 37.2% Abitur, i.e. degree after grade 12-13). Eighty-five participants (62.0%) were diagnosed with RRMS, 37 (27.0%) with SPMS, and 15 (10.9%) with PPMS [23]. Participants have been living with the disease on average for

70 17.5 years ($SD = 9.6$) with mostly mild to moderate disease symptoms (EDSS =
4.0, $SD = 2.1$, range: 1.0-8.0, EDSS = Expanded Disability Status Scale [24]).
Sixty-two participants were at least partially retired from work. Among these
participants, 51 participants stated disability and 11 participants stated age as
the reason for their retirement. A comparison with an unselected MS patient
75 sample at the Kliniken Schmieder suggests that the recruited participants were
representative for the patient population.

2.2. Memory tests

We assessed working memory and semantic memory with the inventory for
memory diagnostics (Inventar zur Gedächtnisdiagnostik, IGD [25]), an estab-
80 lished normed German memory battery.

2.2.1. Working memory

The four working memory tests (subtests A2-A5) measure the ability to
shortly store information, to manipulate it, and to shift attention between dif-
ferent sources of information. In the digit span task, a sequence of digits is read
85 out to each participant and the participant has to remember the digits in correct
order. In the verbal working memory task, the participant has to remember all
words containing the letter "r" from a list of 14 words read out to her. In the
visual working memory task, participants remember the position and alignment
of seven lines and later place the lines into a blank square. In the executive
90 control task, nine boxes contain a different number of grey and black triangles
and circles. Participants have to count and remember the number of grey items
in each box with the color of triangles and circles alternating between boxes.

2.2.2. Semantic memory

The semantic memory tests (subtests B1-B4) measure previously acquired
95 semantic knowledge across four domains: object, concept, word, and factual
knowledge. For instance, the object knowledge task asks participants to map
typical features (e.g., "weight": "100kg", "12kg", "1g", "200g", "1000kg",

"30kg") onto five different objects (e.g., "feather", "car", "bike", "refrigerator", "pocketbook").

100 2.3. Decision-making competence

We translated the A-DMC to German according to a committee approach. A professional interpreter back-translated the German version to English. As in the Italian version, we modified some items because of cultural differences [7]. A sample of healthy relatives ($n = 87$, 51 females, $M_{Age} = 48.9$, SD_{Age}
105 $= 14.4$) completed the translated A-DMC in paper-pencil format. Reliabilities were comparable to previous studies [8], ranging from Cronbach's $\alpha = .51$ for Resistance to Sunk Costs to $\alpha = .78$ for Resistance to Framing.

2.3.1. Resistance to Framing

How a decision problem is described or framed often affects decisions in
110 formally equivalent problems [26]. The Resistance to Framing task measures how resistant people are to framing with seven attribute framing and seven risky-choice problems. In attribute framing, for instance, the effectiveness of a new condom is described with a 95% success rate in the positive frame and with a 5% failure rate in the negative frame. Participants express endorsement on a
115 6-point Likert scale, ranging for instance from "Insecure" to "Secure". A lower mean absolute difference between the ratings for positive and negative frames indicates a higher resistance to the framing effect (reverse coded).

2.3.2. Under/Overconfidence

The Under/Overconfidence task measures the degree to which the confidence
120 in one's own knowledge reflects also its accuracy. Participants answered 34 true/false general knowledge statements (e.g., "There is no way to improve your memory.") and indicated how confident they were of their answer on a scale from 50% ("just guessing") to 100% ("absolutely sure"). A smaller absolute difference between the percentage of correct answers and average confidence reflects less
125 under/overconfidence.

2.3.3. *Applying Decision Rules*

The Applying Decision Rules task assesses how accurately participants apply a specified decision rule. In ten multi-attribute decisions, participants choose between fictitious DVD players with different features (e.g., sound quality) according to a predefined decision rule. The complexity of the decision rules varies from rules considering only one attribute (e.g. sound quality) to rules integrating information from all presented attributes. Task performance is measured as the proportion of correctly chosen DVD-Players.

2.3.4. *Consistency in Risk Perception*

Participants judge the probability of ten events (e.g., dying in a terrorist attack) happening within a timespan of one and five years on a scale from 0% ("no chance") to 100% ("certain"). Probability judgments are scored based on their agreement with probability principles. For instance, participants should judge the probability for an event happening within the next year as lower as the probability of the same event happening within the next five years. Performance is evaluated by the proportion of correctly applied probability principles to the 20 event pairs.

2.3.5. *Resistance to Sunk Costs*

Normatively, one should ignore unrecoverable past investments and concentrate on the future consequences of a decision. One's ability to ignore prior invested unrecoverable financial and time costs (sunk costs) is measured by the Resistance to Sunk Costs scale (e.g., "...you ordered a big dessert..., after a few bites you find you are full: would you be more likely to eat more or to stop eating it?"). In ten problems, participants express a preference for the sunk-cost option (e.g., "most likely to continue eating") compared to the normatively correct option (e.g., "most likely to stop eating") on a 6-point Likert scale. Performance is calculated as the average rating for the normatively correct option.

2.4. Clinical Assessments

Disability was assessed by experienced neurologists with the Expanded Disability Status Scale (EDSS [24]). Medical data was collected from the clinical record. The subjective severity of cognitive fatigue was assessed with the cognitive functioning subscale from the Fatigue Scale for Motor and Cognitive Functions (FSMC [27]); the severity of a depressive disorder was measured with the Rasch-based Depression Screening (DESC-II [28]).

2.5. Procedure

Participants gave written informed consent in line with the Declaration of Helsinki after reading the study description on an information sheet and a personal meeting with one researcher. Participants were tested in two sessions in their room. Testing times matched the participants' best daily performance. In the first session, participants were first tested on working memory, next semantic memory, and finally filled out the depression and cognitive fatigue scales. In the second session, participants filled out the A-DMC questionnaire in the order: (1) positively framed Resistance to Framing, (2) Under/Overconfidence, (3) Applying Decision Rules, (4) Consistency in Risk Perception, (5) Resistance to Sunk Costs, (6) negatively framed Resistance to Framing. Participants with physical problems received assistance in filling out the questionnaires. Participants received feedback about their test performance if desired.

2.6. Analysing the relationship between memory performance and decision making

To understand to what degree memory predicts decision making in individuals with MS, we first established a measurement model for "working memory" and "semantic memory" within a confirmatory factor analysis. This measurement model specified which memory tests measure the latent constructs "working memory" and "semantic memory" and estimated how strongly working memory and semantic memory are correlated.

In a next step, we tested in a regression-based structural model which memory construct predicted decision making as measured with the A-DMC subtest [29, 8, 30]. In line with previous studies [17, 8], we predicted that working memory facilitates decisions in cognitive demanding tasks (Resistance to Framing, Under/Overconfidence, Applying Decision Rules), whereas semantic memory helps knowledge-based decisions (Consistency in Risk Perception, Resistance to Sunk Costs) or tasks requiring the comprehension of complex instructions (Applying the Decision Rules). To test these assumptions, we compared the candidate model that, for instance, postulated a relationship between working memory and resistance to framing, against two competitors: A null model specifying that memory does not predict resistance to framing and a full-path model specifying that working memory and semantic memory contribute to resistance to framing. If only working memory predicts resistance to framing, then this candidate model should outperform the null model, but adding semantic memory as a predictor should not further improve model fit.

Regression weights were tested using χ^2 difference tests that compared the model with the hypothesised relationship to competitors without that relationship. All analyses were controlled for age and education ⁵. Because of deviations from multivariate normality, we estimated all models using a maximum likelihood estimator with robust standard errors (MLM) and Satorra-scaled χ^2 values (scaling factor, SF, for χ^2 difference tests, [31]). Model fit was evaluated with several fit indices (reference thresholds in brackets): χ^2 , the standardized root-mean-square residual (SRMR < .06), the comparative fit index (CFI > .95), and the root-mean-square error of approximation (RMSEA < .05, [32, 30]).

⁵Controlling in addition for EDSS did not alter any major conclusion. Semantic memory predicted slightly worse how accurately participants followed decision rules when accounting for individual differences in working memory, $\Delta\chi^2(1) = 2.7$, $p = .102$, but the estimated coefficient did not change in magnitude, $b = 0.25$ (0.13).

205 3. Results

3.1. Descriptive statistics

Normed percentile ranks based on the inventory for memory diagnostics indicated that working memory was below average in participants ($M = 34.2$ %, $SD = 31.0$, table 1 for descriptive statistics for all measures), but semantic
210 memory was not impaired ($M = 47.5$ %, $SD = 36.5$). Our participants with diagnosed MS performed similar to healthy participants on decision making tasks [6, 8]. Most participants reported moderate ($N = 21$, 15.3%) or severe ($N = 73$, 53.3 %) cognitive fatigue symptoms and only a few participants did not experience any ($N = 27$, 19.7%) or mild symptoms ($N = 16$, 11.7%). 63
215 participants could be classified as experiencing a depressive episode according to the Rasch-based depression screening (46%).

3.2. Measuring working and semantic memory

We expected that all working memory tests relate to the construct "working memory" and all semantic memory tests relate to the construct "semantic mem-
220 ory". In addition, participants with a better working memory may also possess a better semantic memory, that is, "working memory" and "semantic memory" are moderately correlated [17, 8]. Although this measurement model outperformed a model assuming that working and semantic memory are uncorrelated, $\Delta\chi^2(1) = 28.5$, $p < .001$, or a model assuming that working and semantic mem-
225 ory are identical, $\Delta\chi^2(1) = 10.2$, $p < .001$ (see Table 2 for fit indices), not all fit indices indicated a satisfying fit. Modification indices suggested an insufficient discriminant validity of word knowledge (MI = 12.9) so that we excluded word knowledge. The revised model without word knowledge proposed that participants with a better working memory more successfully retrieve knowledge from
230 semantic memory (Figure 1).

3.3. Predicting decision making with memory

In most cognitively demanding tasks, participants with higher working memory scored higher on decision making competence (see Table 3 for model fits).

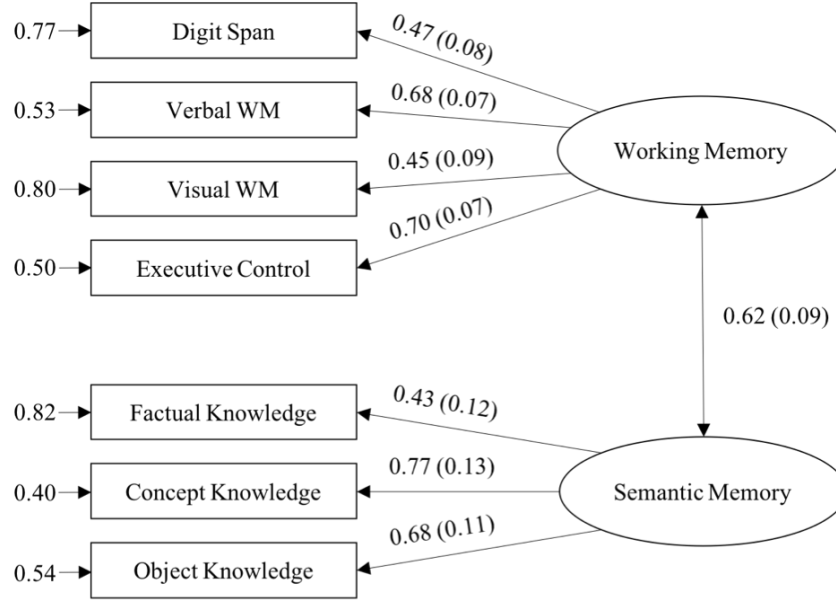


Figure 1: The revised measurement model suggesting a correlation between working memory and semantic memory. Arrows indicate standardized factor loadings; double-headed arrows indicate correlations; residual variances are displayed at the arrows to the memory tests. Standard errors in parentheses.

Participants with higher working memory more likely resisted framing effects, $\Delta\chi^2(1) = 12.2, p < .001$, but semantic memory did not increase resistance to framing further, $\Delta\chi^2(1) = 1.7, p = .189$. Likewise, in the over-/underconfidence task, working memory predicted how well participants' confidence ratings represented their knowledge, $\Delta\chi^2(1) = 6.2, p = .01$. Yet, predicting over-/underconfidence jointly with working and semantic memory further improved the prediction $\Delta\chi^2(1) = 15.2, p < .001$. Regression weights in this model suggest that participants with a better semantic memory successfully adjust their confidence ratings to the knowledge they possess, but working memory contributes little to well-calibrated confidence ratings. Finally, applying decision rules should draw on working memory and semantic memory. In line with this idea, participants with a higher working memory applied decision rules more accurately, $\Delta\chi^2(1) = 34.2, p < .001$, as did participants with a better semantic memory, $\Delta\chi^2(1)$

= 32.9, $p < .001$. Jointly considering both memory abilities further improved model fit, $\Delta\chi^2(1) = 5.8$, $p = .016$, but the higher regression weight for working memory indicates that working memory may be more important for following
250 decision rules.

In knowledge-based tasks, participants with a better semantic memory perceived risks more consistently, $\Delta\chi^2(1) = 9.5$, $p < .002$, but participants with a higher working memory did not, $\Delta\chi^2(1) = 3.7$, $p = .054$. Finally, a better semantic memory did not help to resist sunk costs, $\Delta\chi^2(1) = 0.5$, $p = .497$, nor
255 did working memory explain better why people resist sunk costs, as indicated by the unsatisfying model fits. Thus, memory did not contribute to resisting sunk costs.

3.4. Cognitive fatigue and depression as predictors for memory

Depression and cognitive fatigue were expected to impede memory and, in
260 turn, to be negatively correlated with decision making skills. Yet, neither cognitive fatigue, $\Delta\chi^2(2) = 2.8$, $p = .240$, nor depression, $\Delta\chi^2(2) = 1.4$, $p = .477$, predicted working and semantic memory (Table 4). Consequently, depression and cognitive fatigue unlikely explain why lower memory performance is associated with lower decision making skills in individuals with MS.

265 4. Discussion

Making informed, competent treatment and life decisions may pose a challenge for individuals with MS [33]. Facilitating those decisions has recently attracted more attention because decision making skills affect treatment compliance and adherence [5, 34, 35]. This study investigated to what degree memory
270 deficits carry over to decision making in individuals with MS. Using an established memory battery [25], we replicated previous findings that individuals with MS show working memory deficits, whereas semantic memory is less impaired [2]. Working memory was associated with semantic memory, matching findings in a healthy sample [8].

275 Compared to previous studies, we assessed decision making competence with
the broad, multidimensional A-DMC battery [6]. Our analyses revealed that
limited working memory capacity predicted resistance to framing as well as the
capacity to follow decision rules [8]. In combination, these results indicate that
working memory deficits in MS may carry over to decisions that require to
280 focus on relevant information and suppress irrelevant information. Framing and
communicating decision alternatives, such as treatment options, thoroughly may
thus be particularly important for MS patients with known working memory
impairments.

Semantic memory predicted over- and underconfidence, consistency in risk
285 perception as well as applying decision rules. Replicating previous findings
[8], these associations highlight that every-day decision tasks often demand re-
trieving previously learned knowledge from long-term memory, ranging from
understanding complex instructions to judging the likelihood of events. It is
less clear why better semantic memory predicted a more accurate assessment of
290 one's own knowledge. Potentially, raised awareness to their own memory fail-
ures helps individuals with good semantic memory to still keep track of their
knowledge, but once semantic memory worsens, they are unable to assess their
lack of knowledge. In a shared decision-making setting, this might imply that
patients' ability to monitor their disease-related knowledge worsens as a function
295 of cognitive decline.

In contrast to previous work [36, 8], we did not find any association between
memory and resisting sunk costs. Potentially, depression in MS suppressed the
affect-laden processes underlying sunk cost effects [37]. This result might be
clinically relevant, as depressed patients might give up earlier on treatments
300 that do not show fast initial success.

4.1. Limitations and future research

Although the majority of individuals with MS reported cognitive fatigue
and depressive symptoms, our results do not provide any evidence that those
clinical symptoms further aggravate memory impairments. These absent links

305 resonate well with the notion that depression is not causally linked to cognitive abilities in MS [19, 20] and that cognitive fatigue does not consistently predict cognitive abilities [21]. Still, objective measures of fatigue could provide a more fine-grained picture of the relationship between decision skills and memory impairments in individuals with MS.

310 In our study, we followed a cross-sectional confirmatory approach to test which memory components underlie decision making in individuals with MS. This approach comes at the cost of a comprehensive neurological and pharmacological assessment that may further shed light on the causes of memory and decision making problems within MS. Brain atrophy as well as widespread microscopic brain tissue damage have been associated with distinct patterns of
315 cognitive decline [38, 39] and may thus also impact differentially on decision making. Unfortunately, our study lacks the necessary structural MRI data to further investigate the neurological underpinnings of decision making deficits in MS. In addition, it would be worthwhile to note if the memory impairments in
320 MS give rise to more severe impairments in decision making than in a healthy control group, a conclusion that can only be drawn from a design with a healthy control group. Finally, we did not aim to cover all memory components. Future work may more thoroughly investigate to what degree measures of episodic memory or executive functioning, such as inhibition, contribute to accurate decisions. This may help to design treatment information in such a way that
325 individuals with MS can process this information easily and reach a decision consistent with their goals and needs. Such a more naturalistic design may further shed light on how integrating information in working memory affects clinically relevant treatment decisions in MS.

330 5. Conclusion

Memory impairments are frequently reported in MS. Our study suggests that those impairments reach out to higher-order cognitive functions, such as decision making. Improving treatment decisions in MS thus likely benefits from

acknowledging the patients' memory limits and match the information provided
335 to the patient's memory abilities.

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References

- [1] M. P. Amato, G. Ponziani, G. Pracucci, L. Bracco, G. Siracusa, L. Amaducci, Cognitive Impairment in Early-Onset Multiple Sclerosis, *Archives of Neurology* 52 (2) (1995) 168. doi:10.1001/archneur.1995.00540260072019.
345 URL <http://archneur.jamanetwork.com/article.aspx?doi=10.1001/archneur.1995.00540260072019>
- [2] N. D. Chiaravalloti, J. DeLuca, Cognitive impairment in multiple sclerosis, *The Lancet Neurology* 7 (12) (2008) 1139–1151. doi:10.1016/S1474-4422(08)70259-X.
350 URL [http://dx.doi.org/10.1016/S1474-4422\(08\)70259-X](http://dx.doi.org/10.1016/S1474-4422(08)70259-X)
- [3] S. M. Rao, J. Grafman, D. DiGiulio, W. Mittenberg, E. Al, Memory dysfunction in multiple sclerosis: Its relation to working memory, semantic encoding, and implicit learning., *Neuropsychology* 7 (3) (1993) 364–374. doi:10.1037/0894-4105.7.3.364.
355 URL <http://doi.apa.org/getdoi.cfm?doi=10.1037/0894-4105.7.3.364>
- [4] K. Rahn, B. Slusher, A. Kaplin, Cognitive impairment in multiple sclerosis: a forgotten disability remembered., *Cerebrum*.

- 360 [5] E. D’Amico, C. Leone, F. Patti, Disability may influence patient willingness to participate in decision making on first-line therapy in multiple sclerosis, *Functional Neurology* 31 (1) (2016) 21–23. doi:10.11138/FNeur/2016.31.1.021.
- [6] W. Bruine de Bruin, A. M. Parker, B. Fischhoff, Individual differences in adult decision-making competence., *Journal of personality and social psychology* 92 (5) (2007) 938–956. doi:10.1037/0022-3514.92.5.938.
- 365 [7] F. Del Missier, T. Mäntylä, W. B. de Bruin, W. Bruine de Bruin, Executive functions in decision making: An individual differences approach, *Thinking & Reasoning* 16 (2) (2010) 69–97. doi:10.1080/13546781003630117.
- 370 URL <http://www.tandfonline.com/doi/abs/10.1080/13546781003630117>
<http://dx.doi.org/10.1080/13546781003630117>
- [8] F. Del Missier, T. Mäntylä, P. Hansson, W. Bruine de Bruin, A. M. Parker, L.-G. G. Nilsson, W. B. De Bruin, A. M. Parker, L.-G. G. Nilsson, The Multifold Relationship Between Memory and Decision Making: An Individual-Differences Study., *Journal of Experimental Psychology: Learning, Memory, and Cognition* 39 (5) (2013) 1344–1364. doi:10.1037/a0032379.
- 375 URL <http://www.ncbi.nlm.nih.gov/pubmed/23565790>
<http://doi.apa.org/getdoi.cfm?doi=10.1037/a0032379>
- 380 [9] J. A. Hoffmann, B. von Helversen, J. Rieskamp, Pillars of Judgment: How Memory Abilities Affect Performance in Rule-Based and Exemplar-Based Judgments, *Journal of Experimental Psychology: General* 143 (6) (2014) 2242–2261. doi:10.1037/a0037989.
- [10] S. Lewandowsky, Working memory capacity and categorization: Individual differences and modeling., *Journal of Experimental Psychology: Learning, Memory, and Cognition* 37 (3) (2011) 720–738. doi:10.1037/a0022639.
- 385 URL <http://doi.apa.org/getdoi.cfm?doi=10.1037/a0022639>

- [11] A. M. Parker, W. Bruine de Bruin, B. Fischhoff, J. Weller, Robustness of Decision-Making Competence: Evidence from Two Measures and an 11-Year Longitudinal Study, *Journal of Behavioral Decision Making* 31 (3) (2018) 380–391. doi:10.1002/bdm.2059.
- [12] M. F. Farez, L. Crivelli, R. Leiguarda, J. Correale, Decision-making impairment in patients with multiple sclerosis: a case-control study, *BMJ Open* 4 (7) (2014) e004918—e004918. doi:10.1136/bmjopen-2014-004918.
URL <http://bmjopen.bmj.com/cgi/doi/10.1136/bmjopen-2014-004918>
- [13] N. Muhlert, V. Sethi, L. Cipolotti, H. Haroon, G. J. M. Parker, T. Yousry, C. Wheeler-Kingshott, D. Miller, M. Ron, D. Chard, The grey matter correlates of impaired decision-making in multiple sclerosis, *Journal of Neurology, Neurosurgery & Psychiatry* 86 (5) (2015) 530–536. doi:10.1136/jnnp-2014-308169.
URL <http://jnnp.bmj.com/lookup/doi/10.1136/jnnp-2014-308169>
- [14] J. Kleeberg, L. Bruggimann, J. M. Annoni, G. Van Melle, J. Bogousslavsky, M. Schluep, Altered decision-making in multiple sclerosis: A sign of impaired emotional reactivity?, *Annals of Neurology* 56 (6) (2004) 787–795. doi:10.1002/ana.20277.
- [15] S. Simioni, C. Ruffieux, J. Kleeberg, L. Bruggimann, R. A. Du Pasquier, J. M. Annoni, M. Schluep, Progressive decline of decision-making performances during multiple sclerosis, *Journal of the International Neuropsychological Society* 15 (2) (2009) 291–295. doi:10.1017/S1355617709090262.
- [16] R. C. Atkinson, R. M. Shiffrin, Human Memory: A Proposed System and its Control Processes, in: *The psychology of learning and motivation*, Vol. 2, 1968, pp. 89–195. doi:10.1016/S0079-7421(08)60422-3.
URL <http://books.google.com/books?hl=en&lr=&id=SVxyXuG73wwC&oi=fnd&pg=PA89&dq=Human+Memory:+A+Proposed+System+and+its+Control+Processes&ots=>

CxMavwMT6u{&}sig=EgQNkFa{ }7{ }48D0GVRtDUhR1{ }rashttp:
//linkinghub.elsevier.com/retrieve/pii/S0079742108604223

- 420 [17] F. Del Missier, T. Mantyla, W. Bruine de Bruin, Decision-making Competence, Executive Functioning, and General Cognitive Abilities, *The Journal of Behavioral Decision Making* 25 (February 2011) (2012) 331–351. doi:10.1002/bdm.731.
- [18] A. Koriatic, S. Lichtenstein, B. Fischhoff, Reasons for confidence, *Journal of Experimental Psychology: Human Learning and Memory* 6 (2) (1980) 2.
425 URL <http://linkinghub.elsevier.com/retrieve/pii/S0096151507603168>
- [19] P. A. Arnett, Longitudinal consistency of the relationship between depression symptoms and cognitive functioning in multiple sclerosis, *CNS Spectrums* 10 (5) (2005) 372–382. doi:10.1017/S1092852900022744.
- 430 [20] H. A. Demaree, E. Gaudino, J. DeLuca, The relationship between depressive symptoms and cognitive dysfunction in multiple sclerosis, *Cognitive Neuropsychiatry* 8 (3) (2003) 161–171. doi:10.1080/13546800244000265.
- [21] K. Hanken, P. Eling, H. Hildebrandt, Is there a cognitive signature for MS-related fatigue?, *Multiple Sclerosis Journal* 21 (4) (2015) 376–381. doi:
435 10.1177/1352458514549567.
URL <http://journals.sagepub.com/doi/10.1177/1352458514549567>
- [22] C. H. Polman, S. C. Reingold, B. Banwell, M. Clanet, J. A. Cohen, M. Filippi, K. Fujihara, E. Havrdova, M. Hutchinson, L. Kappos, F. D. Lublin, X. Montalban, P. O’Connor, M. Sandberg-Wollheim, A. J. Thompson,
440 E. Waubant, B. Weinshenker, J. S. Wolinsky, Diagnostic criteria for multiple sclerosis: 2010 Revisions to the McDonald criteria, *Annals of Neurology* 69 (2) (2011) 292–302. doi:10.1002/ana.22366.
URL <http://doi.wiley.com/10.1002/ana.22366>

- [23] F. D. Lublin, S. Reingold, Defining the clinical course of multiple sclerosis results of an international survey, *Neurology* 46 (1996) 907–911.
- [24] J. F. Kurtzke, Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS), *Neurology* 33 (11) (1983) 1444.
arXiv:arXiv:1011.1669v3, doi:10.1212/WNL.33.11.1444.
URL <http://www.neurology.org/cgi/doi/10.1212/WNL.33.11.1444>
- [25] G. Baller, M. Brand, E. Kalbe, J. Kessler, IGD. Inventar zur Gedächtnisdiagnostik, Hogrefe, Göttingen, Germany, 2006.
- [26] A. Tversky, D. Kahneman, The Framing of Decisions and the Psychology of Choice, *Science* 211 (4481) (1981) 453–458.
doi:10.1126/science.7455683.
URL http://link.springer.com/chapter/10.1007/978-1-4613-2391-4_{_}2
- [27] I. K. Penner, C. Raselli, M. Stöcklin, K. Opwis, L. Kappos, P. Calabrese, The Fatigue Scale for Motor and Cognitive Functions (FSMC): validation of a new instrument to assess multiple sclerosis-related fatigue, *Multiple Sclerosis Journal* 15 (12) (2009) 1509–1517. doi:10.1177/1352458509348519.
URL <http://journals.sagepub.com/doi/10.1177/1352458509348519>
- [28] T. Forkmann, M. Böcker, M. Wirtz, S. Gauggel, C. Norra, Raschbasiertes Depressionsscreening, 2011.
- [29] J. C. Anderson, D. W. Gerbing, Structural equation modeling in practice: A review and recommended two-step approach, *Psychological Bulletin* 103 (3) (1988) 411–423. doi:10.1037/0033-2909.103.3.411.
URL http://www.cob.unt.edu/slides/Paswan/BUSI6280/Anderson_{_}Gerbing_{_}1988.pdf<http://www.fdewb.unimaas.nl/meteor/EDEN/MikeBrady/AndersonandGerbing1988.pdf><http://doi.apa.org/getdoi.cfm?doi=10.1037/0033-2909.103.3.411>

- [30] R. B. Kline, Principles and Practice of Structural Equation Modeling, 3rd Edition, Guilford Press, New York, NY, 2011.
URL <http://books.google.com/books?hl=en&lr=&id=mGf3Ex59AX0C&oi=fnd&pg=PR1&dq=Principles+and+Practice+of+Structural+Equation+Modeling&ots=xvNv-4Qc10&sig=mr7InsYsaTanqGxIQTF7PDtEfhg>
- [31] A. Satorra, P. Bentler, A scaled difference Chi-square test statistic for moment structure analysis, *Psychometrika* 66 (4) (2001) 507–514.
URL <http://www.springerlink.com/index/Q4U780616R702384.pdf>
- 475 [32] D. Iacobucci, Structural equations modeling: Fit Indices, sample size, and advanced topics, *Journal of Consumer Psychology* 20 (1) (2010) 90–98.
doi:10.1016/j.jcps.2009.09.003.
URL <http://linkinghub.elsevier.com/retrieve/pii/S1057740809001120>
- 485 [33] S. S. Cofield, Nina Thomas, T. Tyry, R. J. Fox, A. Salter, Shared decision making and autonomy among us participants with multiple sclerosis in the NARCOMS registry, *International Journal of MS Care* 19 (6) (2017) 303–312. doi:10.7224/1537-2073.2016-091.
- [34] W. Gaissmaier, H. Giese, M. Galesic, R. Garcia-Retamero, J. Kasper,
490 I. Kleiter, S. G. Meuth, S. Köpke, C. Heesen, Numeracy of multiple sclerosis patients: A comparison of patients from the PERCEPT study to a German probabilistic sample, *Patient Education and Counseling* 101 (1) (2018) 74–78. doi:10.1016/j.pec.2017.07.018.
URL <http://dx.doi.org/10.1016/j.pec.2017.07.018https://linkinghub.elsevier.com/retrieve/pii/S0738399117304317>
- 495 [35] G. K. Reen, E. Silber, D. W. Langdon, Multiple sclerosis patients ’ understanding and preferences for risks and benefits of disease-modifying drugs: A systematic review, *Journal of the Neurological Sciences* 375 (2017) 107–

122. doi:10.1016/j.jns.2016.12.038.

500 URL <http://dx.doi.org/10.1016/j.jns.2016.12.038>

- [36] W. Bruine de Bruin, F. D. Missier, I. P. I. P. Levin, F. Del Missier, I. P. I. P. Levin, Individual Differences in Decision-making Competence, *Journal of Behavioral Decision Making* 330 (4) (2012) 329–330. doi:10.1002/bdm. URL <http://doi.wiley.com/10.1002/bdm.753><http://onlinelibrary.wiley.com/doi/10.1002/bdm.753/abstract>

- 505 [37] K. Szanto, W. B. de Bruin, A. M. Parker, M. N. Hallquist, P. M. Vanyukov, A. Y. Dombrovski, Decision-Making Competence and Attempted Suicide, *The Journal of Clinical Psychiatry* 76 (12) (2015) e1590—e1597. doi:10.4088/JCP.15m09778. URL <http://www.psychiatrist.com/jcp/article/pages/2015/v76n12/v76n1203.aspx>

- [38] M. P. Amato, E. Portaccio, B. Goretti, V. Zipoli, M. Battaglini, M. L. Bartolozzi, M. L. Stromillo, L. Guidi, G. Siracusa, S. Sorbi, A. Federico, N. De Stefano, Association of Neocortical Volume Changes With Cognitive Deterioration in Relapsing-Remitting Multiple Sclerosis, *Archives of Neurology* 64 (8) (2007) 1157–1161.

- 520 [39] C. Vinciguerra, A. Giorgio, J. Zhang, I. Di Donato, M. L. Stromillo, R. Tappa Brocci, A. Federico, M. T. Dotti, N. De Stefano, Peak width of skeletonized mean diffusivity (PSMD) as marker of widespread white matter tissue damage in multiple sclerosis, *Multiple Sclerosis and Related Disorders* 27 (October 2018) (2019) 294–297. doi:10.1016/j.msard.2018.11.011. URL <https://doi.org/10.1016/j.msard.2018.11.011>

Table 1: Descriptive Statistics for Memory, Decision-Making Competence, and Clinical Measures

Measure	<i>M</i>	<i>SD</i>	Min	Max	Skewness	Kurtosis	Reliability
Working memory							.67 [◇]
Digit Span	7.6	1.9	3	12	0.1	- 0.3	
Verbal WM	15.2	3.6	2	21	- 0.9	0.7	
Visual WM	12.1	5.0	1	21	- 0.2	- 1.0	
Executive Control	14.5	5.7	2	25	- 0.1	- 0.8	
Semantic memory							.67 [◇]
Object knowledge	97.2	3.4	68	100	- 5.0	38.4	
Concept knowledge	97.3	4.2	73	100	- 2.3	7.7	
Word knowledge	18.4	1.9	11	20	- 1.8	3.3	
Factual knowledge	86.5	8.2	62	99	- 0.8	0.2	
A-DMC							
Resistance to Framing	3.9	0.7	1.2	5.0	- 0.9	1.5	.72*
Under/Overconfidence	.90	.07	.71	1.00	- 0.7	- 0.4	.56*
Applying Decision Rules	.67	.16	.13	.93	- 0.5	0.1	.68*
Consistency in Risk Perception	.77	.13	.35	1.00	- 0.6	0.3	.59*
Resistance to Sunk Costs	4.5	0.7	2.30	6.00	- 0.5	0.0	.59*
Clinical assessments							
Cognitive Fatigue	32.1	10.0	10	49	- 0.5	- 0.9	.93*
Depression	11.6	8.4	0	39	0.7	0.0	.93*
EDSS	4.0	2.1	1	8	0.2	- 1.1	— [†]

Note. WM = working memory; A-DMC = Adult Decision-Making Competence; EDSS = Expanded Disability Status Scale. [◇] Composite reliability; * Cronbach's α ; [†] EDSS score taken from medical record

Table 2: Confirmatory Factor Analysis of Memory

Model	SRMR	RMSEA	CFI	χ^2	<i>df</i>	SF	<i>p</i>
WM + SM	.06	.05	.93	25.9	19	1.3	.133
WM + SM (uncorrelated)	.21	.13	.52	68.9	20	1.3	< .001
Unitary	.07	.06	.89	31.6	20	1.3	.047
WM + SM (revised)	.05	.04	.97	15.4	13	1.0	.282

Note. WM = working memory; SM = semantic memory; SRMR = standardized root-mean-squared residual; RMSEA = root-mean-square error of approximation; CFI = comparative fit index; SF = Scaling Factor.

Table 3: Fit Indices for Models Predicting Decision Making with Memory

DM	Model	SRMR	RMSEA	CFI	χ^2	df	SF	p	WM → DM	SM → DM
RCA	FP	.05	.02	.98	19.4	18	1.0	.370	.31 (.13)	.28 (.19)
	WM	.05	.03	.98	20.6	19	1.2	.359	.53 (.13)	—
	Null	.14	.08	.77	36.7	20	1.5	.013	—	—
CAL	FP	.05	.01	1.00	18.1	18	1.1	.452	-.11 (.17)	.52 (.14)
	WM	.07	.07	.86	30.7	19	1.0	.044	.31 (.11)	—
	Null	.11	.08	.80	36.3	20	1.1	.014	—	—
DR	FP	.05	.04	.95	22.7	18	1.1	.201	.43 (.15)	.28 (.13)
	WM	.06	.06	.92	27.0	19	1.0	.104	.65 (.09)	—
	SM	.06	.05	.92	26.5	19	1.2	.116	—	.64 (.08)
	Null	.16	.13	.53	66.8	20	1.2	.001	—	—
RP	FP	.05	.02	.99	19.1	18	1.0	.387	.25 (.14)	.22 (.13)
	SM	.05	.03	.96	21.9	19	1.0	.291	—	.41 (.10)
	Null	.12	.07	.82	34.2	20	1.2	.025	—	—
SC	FP	.06	.07	.85	29.4	18	1.1	.044	-.26 (.14)	.31 (.19)
	SM	.07	.07	.83	31.6	19	1.1	.035	—	.11 (.15)
	Null	.07	.06	.88	29.4	20	1.2	.080	—	—

Note. The endorsed model is indicated in bold. Regression coefficients for memory on the decision task are indicated by →. Standard errors in parentheses. DM = Decision Making Task; RCA = Resistance to Framing; CAL = Under/Overconfidence; DR = Applying Decision Rules; RP = Consistency in Risk Perception; SC = Resistance to Sunk Costs; FP = full-path model; WM = working memory; SM = semantic memory; SRMR = standardized root-mean-squared residual; RMSEA = root-mean-square error of approximation; CFI = comparative fit index.

Table 4: Fit Indices for Models Predicting Memory with the Clinical Assessments

Scale	SRMR	RMSEA	CFI	χ^2	<i>df</i>	SF	<i>p</i>	CA → WM	CA→ SM
Fatigue	.07	.07	.83	42.4	25	1.0	.016	-.11 (.10)	.06 (.08)
Depression	.08	.07	.82	43.6	25	1.0	.012	.05 (.09)	.11 (.10)
Null	.08	.07	.82	45.6	27	1.0	.014	—	—

Note. The endorsed model is indicated in bold. Regression coefficients for clinical assessments on memory are indicated by →. Standard errors in parentheses. CA = Clinical Assessment; WM = working memory; SM = semantic memory; SRMR = standardized root-mean-squared residual; RMSEA = root-mean-square error of approximation; CFI = comparative fit index.